REMARKS

Upon entry of the foregoing amendments, allowed claims 33 and 34 and new claims 49-58 will be pending in the application. Claims 33, 53 and 56 are independent claims. Claims 38, 39 and 42-48 have been cancelled, without prejudice to their inclusion in one or more related applications, solely for the purpose of advancing the prosecution of this application.

New independent claims 53 and 56 have been added, which respectively recite proteins having 80% sequence identity with SEQ ID NO:35 and 90% sequence identity with SEQ ID NO:23 or SEQ ID NO:35. Support for the 80% and 90% homology in claims 53 and 56 is set forth in the application as filed, for example at page 15, lines 11-13. The sequences recited in claims 53 and 56 are the same or subsets of the sequences recited in previously presented claims 39, 47 and 48 and are a subset of the sequences recited in original claim 12, now canceled.

New dependent claims 49, 51, 54 and 57 are directed to pharmaceutical compositions comprising the isolated protein of claims 33, 34, 53 and 56, respectively, and are supported in various locations throughout the application, including claim 16 as originally filed.

New claims 50, 52, 55 and 57 are directed to the pharmaceutical compositions of claims 49, 51, 54 and 56 which are immunogenic. This is likewise supported throughout the application, particularly at page 13, lines 5-7, and original claims 15 and 17, for example.

Since none of the new claims include any new matter, their entry is respectfully solicited.

Cancellation of rejected claims 38, 39 and 42-48 renders moot the former rejections under 35 U.S.C. § 112 (enablement) and § 102 (novelty). Claims 33 and 34 were not rejected on either ground.

The following comments are provided in support of claims 49-58 to obviate any rejections that may be considered by the Examiner.

Novelty

The Examiner has previously relied on Masignani and Peak as being relevant to the novelty of former claims 38, 39 and 42-48.

New claims 53 and 56 are novel over both Masignani and Peak. More particularly, neither Masignani nor Peak teaches or suggests an isolated protein that is at least 90% identical

over the entire length of SEQ ID NOS:23 or 35, as set forth in claim 56. Neither Masignani nor Peak teach or suggest an isolated protein that is at least 80% identical over the entire length of SEQ ID NO:35, as set forth in claim 53.

The closest sequence in Peak is SEQ ID NO:21.

A ClustalW (v.1.4) comparison of this prior art sequence with SEQ ID NO:23 reveals 86.6% identity when comparing the entire sequence of SEQ ID NO:21 with the entire sequence of SEQ ID NO:23.

A ClustalW (v.1.4) comparison of this prior art sequence with SEQ ID NO:35 reveals 77% identity when comparing the entire sequence of SEQ ID NO:21 with the entire sequence of SEQ ID NO:35.

The closest sequence in Masignani is SEQ ID NO:4.

A ClustalW (v.1.4) comparison of this prior art sequence with SEQ ID NO:23 reveals 86.6% identity when comparing the entire sequence of SEQ ID NO:4 with the entire sequence of SEQ ID NO:23.

A ClustalW (v.1.4) comparison of this prior art sequence with SEQ ID NO:35 reveals 77% identity when comparing the entire sequence of SEQ ID NO:4 with the entire sequence of SEQ ID NO:35.

Masignani fragment SEQ ID NO:2 is only about 32% identical to SEQ ID NOS:23 and 35.

Furthermore, neither Masignani nor Peak teaches or suggests the functional aspect of claims 53 and 56 that "*the isolated protein is capable of eliciting an immune response to a plurality of strains of N. meningitides.*" Neither citation was concerned with the construction of NhhA deletion mutants that exclude some of the V region amino acids with the intention of minimizing the production of strain-specific immune responses to an administered NhhA immunogen.

Applicants respectfully submit that claims 53, 56 and 49-54 are novel. Moreover, the cited prior art would not render the subject matter of these claims obvious.

Written Description & Enablement

New claims 53 and 56 comply with both the written description and enablement requirements of 35 U.S.C. § 112, first and second paragraphs.

These claims cover variants (whether naturally occurring or artificially created) which possess a high degree of sequence similarity to SEQ ID NOS:23 and 35 and which possess the functional capability of eliciting an immune response to a plurality of strains of *N. meningitidis*.

The present application (particularly Fig. 1 and Table 1) provides substantial guidance to the skilled person as to which amino acid residues may be deleted or modified and which amino acid residues should be retained in order to satisfy this functional requirement. The Examples provide several recombinant strategies for constructing such isolated proteins. While SEQ ID NOS: 23 and 35 were constructed from the PMC21 clone (SEQ ID NO:1), this approach could be adapted to any of the *N. meningitidis* strain sequences set forth in SEQ ID NOS:2-10. Furthermore, Fig. 1 provides a lineup of these sequences with sufficient information, residue by residue, that would enable a skilled person to readily create variants falling within the scope of claims 53 and 56. These variants could be created simply by utilizing other V (variable) and C (conserved) regions, such as from one or more of the other *N. meningitidis* strain sequences.

Following the guidance and specific alignment as set forth in the application would not require an undue burden of experimentation on the part of a skilled person.

With particular regard to the written description, Applicants submit that the breadth of claims 53 and 56 is not indeterminate and that these genus claims are readily supported by a representative number of species described in the specification.

For example, SEQ ID NO: 35 comprises entire V3, V4, C4 and C5 regions, with part of the C3 region, of PMC21 (SEQ ID NO:1). With reference to Fig, 1, by substituting one or more of the corresponding regions of any of the other *N. meningitidis* strain sequences set forth in SEQ ID NOS:2-10 (as generally suggested in the specification at page 12, lines 5-9) for those of SEQ ID NO:35, the specification provides explicit support for the variants falling within the scope of claims 53 and 56, based on the disclosure in Fig. 1 that provides a lineup of these sequences with sufficient information, residue by residue, of variants falling within the scope of claims 53 and 56.

While the specification did not literally recite each of these variant sequences by sequence, Applicants submit that this type of laborious *ipsis verbis* recitation is not required to provide a proper written description.

Reconsideration and withdrawal of all of the rejections and an early Notice of Allowance of all claims are respectfully solicited.

Respectfully submitted,

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